

Amendments to the Specification

Please delete the paragraph beginning at line 30 and ending at line 31 on page 9 of the specification.

~~FIG. 8 Sequence alignment of mammalian PrP sequences as obtained by the CLUSTAL-W algorithm.~~

Please amend the paragraph beginning at line 26 on page 21 and ending at line 10 on page 22 of the specification, as follows:

Large differences in the activation enthalpies of the PrP to PrP^β conversion are observed between the two groups of mammalian prion proteins, including human and bovine PrP, and elk, pig, dog and mouse PrP, respectively (Table 1). The relatively low activation entropies of intact human and bovine PrP argue that the transition state(s) is less unfolded compared to the other prion proteins. Moreover, from the calculated free energy values of conversion and the corresponding reaction rate constants, estimated at 37°C, it turns out that spontaneous conversion in human and bovine PrP is about 600 times faster than in e.g. mouse PrP. Notably, human and bovine PrP are mostly similar with regard to the amino acid sequence and the three-dimensional structure (Lopez Garcia et al., 2000). As the only difference in the conversion reactions is the amino acid sequence of PrP, the variations in kinetic parameters must be rationalized on the basis of species-specific amino acid variations. Consistent sequence variations between the two aforementioned PrP groups are found only in position 155, where human and bovine PrP contain a histidine as compared to tyrosine in the

other prion proteins (~~FIG. 8~~).

Please amend the paragraph beginning at line 12 and ending at line 24 on page 22 of the specification, as follows:

~~FIG. 8 shows the~~ The sequence alignment of mammalian PrP sequences as obtained by the CLUSTAL W algorithm (version 1.8; (Thompson, J. D., Higgins, D. G. and Gibson, T. J. (1994) Clustal-W--Improving the Sensitivity of Progressive Multiple Sequence Alignment through Sequence Weighting, Position-Specific Gap Penalties and Weight Matrix Choice. Nucleic Acids Research, 22, 4673-4680) is ordered with increasing activation enthalpy of conversion (see Table 1) from top to bottom. ~~The identities of individual sequences are indicated on the left. At the top, secondary structure elements of human PrP (Zahn, R., Liu, A., Luhrs, T., Riek, R., von Schroetter, C., Lopez Garcia, F., Billeter, M., Calzolari, L., Wider, G. and Wuthrich, K. (2000) NMR solution structure of the human prion protein. Proc Natl Acad Sci USA, 97, 145-150) are indicated: empty boxes, regular secondary; black line, non-regular secondary structure. The residue numbers according to human PrP are indicated at the bottom.~~

Amendments to the Figures

Please delete Figure 8 without prejudice or disclaimer.